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(54) Title: NASAL SPRAY HAVING DEAD SEA SALTS

(57) Abstract: A nasal spray formulation for use with the treatment of rhinitis, sinusitis, epistaxis and post-surgical irrigation. The nasal spray formulation includes the Dead Sea salt or its equivalent. The composition of the Dead Sea salt mixture includes about 31-35 % magnesium halide, about 24-26 % potassium halide, about 4-8 % sodium halide, about 0.4-0.6 % calcium halide, the halide being about 0.3-0.6 % bromide, about 99.4-99.7 % chloride, and may also include about 0.05-0.2 % sulphates, about 0.5-0.2 % insolubles. The salts may comprise about 34-38 % water of crystallization. The spray formulation is about 0.5 to about 5 grams per liter of sterile aqueous solution, contains a buffer, and is essentially free of noxious, organic impurities.

NASAL SPRAY HAVING DEAD SEA SALTS

BACKGROUND OF THE INVENTION

This is a continuation-in-part application of co-pending serial number 09/345,043, filed June 30, 1999. The present invention relates to a nasal spray formulation used in the treatment of conditions involving the nasal cavity and related passageways. Specifically, the formulation utilizes Dead Sea salts or analogous combinations to assist in the treatment of rhinitis, sinusitis, epistaxis, post-surgical irrigation and the like.

The Dead Sea is one of the most saline lakes in the world. It lies between the hills of Judaea to the west and the Transjordanian plateaus to the east. The Jordan River flows from the north into the Dead Sea. About 2.5 million years ago, heavy stream flow into the lake deposited thick sediments containing shale, clay, sandstone, rock salt, and gypsum. After this, strata of clay, marl, soft chalk, and gypsum fell upon layers of sand and gravel. Having no outlet, the Dead Sea is a "terminal lake" which loses huge amounts of water by evaporation in the hot dry air. The water has evaporated faster than it has been replenished by precipitation over the last 10,000 years, which has resulted in the lake gradually shrinking to its present form. Because of this, bare deposits cover the Dead Sea valley to a thickness of 1 to 4 miles (1.6 to 6.4 km). This water evaporation has also resulted in high concentrations of salts and minerals in a unique composition that is particularly rich in magnesium, sodium, potassium, calcium, bromide and various other minor anions such as, e.g., sulfate. The concentration of salt increases toward the Dead Sea bottom. Down to 130 feet (40m), the temperature varies from 66 ° to 98 ° F (19° to 37° C), and the salinity is slightly less than 300 parts per thousand. At this depth, the water is particularly rich in sulfates and in bicarbonates. There is a transition zone located between 130 and 330 feet (40 and 100 m). The lower waters below 330 ft (100m) have a uniform temperature of about

72°F (22°C) and a higher degree of salinity (approximately 332 parts per thousand). This lower water contains hydrogen sulfide and strong concentrations of magnesium, potassium, chlorine, and bromine. Below this, the deepest waters are saturated with sodium chloride, which is precipitated to the bottom. The lower waters are fossilized--they remain permanently on the bottom because they are very salty and dense. The upper waters date from a few centuries A.D.

Certain references describe the use of the Dead Sea salts, but not in connection with the treatment of nasal conditions. See U.S. Pat. 4,943,432 issued to Biener on July 24, 1990 which mentions the use of Dead Sea salts for use with psoriasis, atopic dermatitis and other skin diseases. See also, U.S. Pat. 5,707,631 issued to Lieberman on January 13, 1998 which describes the use of Dead Sea salts in connection with a herbal composition for use with the treatment of arthritis, blood pressure and Alzheimer's disease.

Further, earlier references list nasal sprays but none which utilizes the Dead Sea salts in the treatment of rhinitis, sinusitis, epistaxis and post-surgical irrigation. See U.S. Pat. 5,840,278 issued to Coleman on November 24, 1998 which indicates use of a nasal spray having a mineral component, a vitamin component and aloe vera for a cold virus remedy. Due to unknown and unexpected complications caused by aloe vera in the treatment of rhinitis, sinusitis, epistaxis and post-surgical irrigation, this formulation may not be best suited for such treatment.

Accordingly, an important object of the invention is to create a formulation in the treatment of conditions of the nasal cavity and passageway.

Another object of the invention is to create a formulation for the treatment of rhinitis, sinusitis, epistaxis and post-surgical irrigation.

Another object of the invention is to create a formulation utilizing the Dead Sea salts for the treatment of rhinitis, sinusitis, epistaxis and post-surgical irrigation.

SUMMARY OF THE INVENTION

In accordance with the above and related objects, the present invention provides a nasal spray formulation for use with the treatment of rhinitis, sinusitis, epistaxis, post-surgical irrigation and the like. The nasal spray formulation includes about 1-5% Dead Sea salt or its equivalent. The composition of the Dead Sea salt mixture includes about 31-35% magnesium halide, about 24-26% potassium halide, about 4-8% sodium halide, about 0.4-0.6% calcium halide, the halide being about 0.3 -0.6% bromide, about 99.4-99.7% chloride. The salt may also include about 0.05-0.2% sulphates, and about 0.5-0.2% insolubles, the latter of which is preferably removed by appropriate filtrations or other means. The salts may comprise about 34-38% water of crystallization. The spray formulation is about 0.5 to about 5.0 grams per liter of aqueous solution. Preferably, the aqueous solution is sterile and contains a buffer, which maintains the pH between 6.5 and 7.5. The spray formulation is preferably also essentially free of noxious organic impurities. "About" in this application means $\pm$ 20%.

Methods for treatment are included in the present invention. In one particular embodiment, the claimed method involves treating symptoms of adverse conditions effecting the nasal cavity and related passageways, which involves identifying a patient with an adverse nasal cavity condition and obtaining a premixed formulation containing a Dead Sea salt or the equivalent formulation and mineral composition in aqueous solution and administering or self-administering an aerosol formed from the formulation at least 1 time a day as symptoms of the patient or individual persist.

A method of producing is also part of the present invention and the formulations which includes dissolving the Dead sea salt in aqueous solution and storing this premixed formulation in a container suitable for nasal aerosol administration.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

The present invention relates to a nasal spray formulation used in the treatment of conditions involving the nasal passageway. Specifically, the formulation utilizes the Dead Sea salts to assist in the treatment of rhinitis, sinusitis, epistaxis, and post-surgical irrigation. Rhinitis is the inflamation of the mucous membranes of the nose. Sinusitis is the inflamation of the sinus. Epistaxis is nose bleed or hemorrahage from the nose.

In a preferred embodiment of the present invention, the Dead Sea salt solution comprises about 0.5 to about 5.0 grams per liter of sterile aqueous solution. Said aqueous solution may be or include a buffer, water, or any other pharmacologically acceptable aqueous mixture. The buffer is to maintain the pH between about 6.5 and 7.5. A buffer is Sodium Phosphate, Potassium Phosphate, Sodium Carbonate, or such other as would be used by those skilled in the art to maintain the pH between 6.5 and 7.5. The composition of the Dead Sea salt mixture includes about 31-35% magnesium halide, about 24-26% potassium halide, about 4-8% sodium halide, about 0.4-0.6% calcium halide. The halide are preferably about 0.3 -0.6% bromide, 99.4-99.7% chloride, and the mixture may also include about 0.05-0.2% sulphates, about 0.5-0.2% insolubles, the later of which are preferably removed by filtrates. The salts may comprise about 34-38% water of crystallization. The formulation is essentially free of noxious organic impurities, such as human waste, dead marine animals, and fossil fuel spillage. "Essentially Free" is defined as no more than harmless, trace quantities.

Although the preferred embodiment of this invention is the use of Dead Sea salt from the Dead Sea, it is understood that one skilled in the art would be able to artificially create a Dead Sea salt. It is also apparent to anyone skilled in the art, that certain pharmacologically accepted ingredients normally found in nasal spray could be added to the

instant nasal spray formulation. However, both of these circumstances are claimed within this application. The claimed invention includes both the use of actual Dead Sea salt and artificially created salt with the same or similar salt and mineral components as Dead Sea salt. Also, the addition of other pharmacologically acceptable nasal spray ingredients does not change the invention claimed in this application.

EXAMPLE

A pilot study has been performed on the Dead Sea salt nasal irrigation. Patients were given verbal and written instructions to use the Dead Sea salt nasal spray formulation for seven days, the first two days were used as a baseline with no treatment, and the patients were to evaluate their nasal stuffiness, watery, itchy eyes, runny nose, sneezing, itchy troat and cough as well as postnasal drainage. On the last five days, they also were instructed to evaluate the Dead Sea salt nasal spray's global efficacy and personal satisfaction. They utilized this medicine through a four ounce nasal squeeze bottle three to four times per day. Instructions were given to mix one teaspoon of Dead Sea salt with two cups of water and then subsequently boil this mixture for five minutes. The mixture used as a nasal spray with two sprays up each nostril three to four times per day was a 2.5% solution with 12 g of the salt crystal in two cups, or 480cc, of water.

Nasal stuffiness was improved by 42%. Watery, itchy eyes were improved by 55.5%. Runny nose was improved by 44%. Global efficacy and personal satisfaction were rated 62.5%. A few patients reported an increase of postnasal drainage by 60-70%. This is thought to be secondary to mobilization of the mucus in sinus cavities. All patients requested that they stay on Dead Sea salt formulation. One patient in particular previously had two endoscopic sinus surgeries and had been placed on IV antibiotics two times. One patient who rated the overall global efficacy as 40% and personal satisfaction as 40% stated

that after desisting use of the Dead Sea salt for five days that it was obvious that it had a greater impact as a treatment than she originally thought. This patient stated that after five days without use of the Dead Sea salt formulation that her hoarseness was back, her ears and throat were bothering her again, her mucous secretions were thicker, and she had sinus pain on the left, all of which had diminished greatly while on the Dead Sea salt irrigation.

One patient tested who had not tried other medical treatment reported the following results: nasal stuffiness-100% improved; eyes-50% improved; runny nose -100% improved; sneezing-82% improved; throat-100% improved; post nasal drainage-100% improved; global efficacy-90% improved; and personal satisfaction-100% improved.

While the invention has been described with a certain degree of particularity, it is manifest that many changes may be made in the arrangement of components without departing from the spirit and scope of this disclosure. It is understood that the invention is not limited to the embodiments set forth herein for purposes of exemplification, but is to be limited only by the scope of the attached claim or claims, including the full range of equivalency to which each element thereof is entitled.

It is understood that the sprit and scope of the present invention is embodied in the following claims.

WHAT IS CLAIMED IS:

1. A nasal spray formulation comprising:

a Dead Sea salt and mineral composition in aqueous solution.

2. The formulation of claim 1 where the aqueous solution is sterile.

3. The formulation of claim 1 defined further as containing a buffer.

4. The formulation of claim 3 where the buffer is to maintain a pH of from about 6.5 to about 7.5.

5. The formulation of claim 1 where the composition is from about 0.5 to about 5 grams per liter of aqueous solution.

6. The formulation of claim 1 where the composition is about 2.5 grams per liter of aqueous solution.

7. The formulation of claim 1 where the composition is essentially free of noxious organic impurities.

8. The formulation of claim 1 wherein said Dead Sea salt and mineral composition is further defined as including about 31-35% magnesium halide, about 24-26% potassium halide, about 4-8% sodium halide, about 0.4-0.6% calcium halide, the halide being about 0.3 -0.6% bromide and about 99.4-99.7% chloride.

9. A method of treating symptoms of adverse conditions affecting the nasal cavity and passageway, the method comprising the steps of identifying patient with an adverse nasal cavity conditions;

a. obtaining a premixed formulation containing a Dead Sea salt and mineral composition in aqueous solution; and

b. administering an aerosol formed from the formulation at least 1 time a day as symptoms of the patient persist.

10. The method of claim 9 wherein said conditions include rhinitis, sinusitis, epistaxis and post-surgical irritation.

11. The method of claim 9 wherein said Dead Sea salt and mineral composition is in sterile aqueous solution.

12. The method of claim 9 wherein said Dead Sea salt and mineral composition in aqueous solution contains a buffer.

13. The method of claim 12 wherein the buffer is to maintain a pH from about 6.5 to about 7.5.

14. The method of claim 9 wherein said Dead Sea salt and mineral composition in aqueous solution is from about 0.5 to about 5 grams of salt per liter of said aqueous solution.

15. The method of claim 9 wherein said Dead Sea salt and mineral composition in aqueous solution is about 2.5 grams of salt per liter of said aqueous solution.

16. The method of claim 9 wherein said Dead Sea salt and mineral composition is further defined as including about 31-35% magnesium halide, about 24-26% potassium halide, about 4-8% sodium halide, about 0.4-0.6% calcium halide, the halide being about 0.3 -0.6% bromide and about 99.4-99.7% chloride.

17. The method of claim 9 wherein said Dead Sea salt and mineral composition in aqueous solution is essentially free of organic impurities.

18. A method for treating symptoms of adverse conditions of the nasal cavity and passageway with a Dead Sea salt and mineral composition in aqueous solution, the method comprising the steps of obtaining a premixed formulation containing a Dead Sea salt mineral composition in aqueous solution; and self administering an aerosol formed from said formulations nasally at least 1 time a day as symptoms persist.

19. The method for claim 18 wherein said conditions include rhinitis, sinusitis, epistaxis and post-surgical irritation.

20. The method of claim 18 wherein a Dead Sea salt mineral composition in aqueous solution is from about 0.5 to about 5 grams per liter of said aqueous solution.

21. The method of claim 18 wherein a Dead Sea salt mineral composition is in sterile aqueous solution.

22. The method of claim 18 wherein a Dead Sea salt mineral composition in aqueous solution contains a buffer.

23. The method of claim 22 wherein the buffer is to maintain a pH of from about 6.5 to about 7.5.

24. The method of claim 18 wherein a Dead Sea salt mineral composition in aqueous solution is about 2.5 grams per liter of said aqueous solution.

25. The method of claim 18 wherein said Dead Sea salt and mineral composition is further defined as including about 31-35% magnesium halide, about 24-26% potassium halide, about 4-8% sodium halide, about 0.4-0.6% calcium halide, the halide being about 0.3 -0.6% bromide and about 99.4-99.7% chloride.

26. The method of claim 18 wherein a Dead Sea salt mineral composition in aqueous solution is essentially free of noxious, organic impurities.

27. A method of producing a nasal spray formulation comprising Dead Sea salt in aqueous solution, the method comprising dissolving Dead Sea salt in aqueous solution and storing this premixed formulation in a container suitable for aerosol nasal administration.

28. The method of claim 27 wherein a Dead Sea salt mineral composition in aqueous

solution is from about 0.5 to about 5 grams per liter of said aqueous solution.

29. The method of claim 27 wherein Dead Sea salt mineral composition in aqueous solution is about 2.5 grams per liter of said aqueous solution.

30. The method of claim 27 wherein Dead Sea salt mineral composition is in sterile aqueous solution.

31. The method of claim 27 wherein Dead Sea salt mineral composition in sterile aqueous solution contains a buffer.

32. The method of claim 31 wherein the buffer is to maintain a pH of from about 6.5 to about 7.5.

33. The method of claim 27 wherein said Dead Sea salt and mineral composition is further defined as including about 31-35% magnesium halide, about 24-26% potassium halide, about 4-8% sodium halide, about 0.4-0.6% calcium halide, and halide being about 0.3 -0.6% bromide and about 99.4-99.7% chloride.

34. The method of claim 27 wherein a Dead Sea salt mineral composition in aqueous solution is essentially free of noxious, organic impurities.

35. A nasal spray formulation comprising a Dead Sea salt and mineral composition having about 31-35% magnesium halide, about 24-26% potassium halide, about 4-8%

sodium halide, about 0.4-0.6% calcium halide, the halide being about 0.3 -0.6% bromide and about 99.4-99.7% chloride, where said Dead Sea salt and mineral composition contains a buffer maintaining a pH from about 6.5 to 7.5 and is from about 0.5 to about 5 grams per liter of sterile aqueous solution and is essentially free of noxious, organic impurities.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/18012

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 33/00, 33/06, 33/14
US CL : 424/663,665,677,678,679,680,681,682,722,723;514/853

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 424/663,665,677,678,679,680,681,682,722,723;514/853

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Remington's Pharmaceutical Sciences (17th Ed. 1985)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	EP 0 937 453 A2 (SCHWARTZ) 25 August 1999 (25.08.1999), pg. 3, lines 26-39, pg. 8, lines 23,24.	1,5-10, 14-20, 24-26
—		
Y,P		2-4, 11-13, 21-23, 27-35
Y	GENNARO, A. R. Remington's Pharmaceutical Sciences (17th Edition) Easton, Pennsylvania: Mack Publishing Company. 1985, pages 1293, 1500, 1662-1677.	2-4, 11-13, 21-23, 27-35

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
11 August 2000 (11.08.2000)	28 AUG 2000
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer Frank Choi Telephone No. (703) 308-1235

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INTERNATIONAL SEARCH REPORT

International application No.
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Continuation of B. FIELDS SEARCHED Item 3: STN/CAS,WEST
search terms: Dead Sea salts,nasal,magnesium,potassium,sodium,calcium,chloride,bromide